REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at (858) 720-5133.

Status of the Claims

Pending claims

Claims 42 to 55, 88 to 96, 101, 103, 106 to 107, 110 to 112 and 115 to 133 are pending.

Claims added in the instant amendment

New claims 134 to 138 are added. Thus, after entry of these amendments, claims 42 to 55, 88 to 96, 101, 103, 106 to 107, 110 to 112 and 115 to 138 are pending and presented for consideration.

Response to the Restriction Requirement

The instant application was restricted to eight (VIII) inventions under 35 U.S.C. §121. Applicants elected Group IV, claims 42-55 and 88-92, drawn to a method of mutagenesis.

Outstanding Rejections

Claims 42 to 55, 88 to 96, 101, 103, 106 to 107, 110 to 112 and 115 to 133, are rejected under 35 U.S.C. §112, as allegedly failing to comply with the enablement requirement. Claims 90 to 92 stand rejected under 35 U.S.C. §112, second paragraph. Claims 88, 89, 93, 95, 96, 101, 103, 106, 107, 110, 112, 115, 117 to 119 and 124 to 133 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Lam, et al., U.S. Patent No. 6,074, 867, issued June 13, 2000, and filed October 15, 1997.

Applicants respectfully traverse all outstanding objections to the specification and rejections of the claims.

Telephonic interview

Applicants thank the Examiner for the telephonic interview of October 26, 2004, calling to inform Applicants that she is the new Examiner and agreeing to have a telephonic interview addressing substantive issues after she has had a chance to review the instant amendment and response.

Support for the claim amendments

The specification sets forth an extensive description of the invention in the new and amended claims. For example, support for claims directed to methods wherein a library of modified small molecules are made from a single starting small molecule compound in a plurality of biocatalytic reactions, and the specific biocatalytic reaction which produces the modified small molecule of desired activity is identified by systematically eliminating each of the biocatalytic reactions used to produce the modified small molecule and then testing the small molecules produced in the portion of the library for the presence or absence of the modified small molecule with the desired activity, can be found, inter alia, on page 71, line 22, to page 72, line 6.

Priority

The Patent Office acknowledged that claims 42, 94, 111, 120 to 123 properly claimed benefit of priority to the parent application, U.S. patent application serial no. (USSN) 08/651,572, filed May 22, 1996, now U.S. Patent No. (USPN) 5,789,228. However, it is alleged that all remaining pending claims 43 to 55, 88 to 93, 95, 96, 101, 103, 106, 107, 110, 112, 115 to 119 and 124 to 133, could only claim benefit of priority to the instant application's disclosure, filed June 22, 2001, which is a CIP of USSN 08/651,572, because there was no specific support in the parent application (see, e.g., paragraph 5, page 3, lines 15 to 16, and, page 4, line 2, of the instant office action of November 3, 2004 ("OA")).

Under 35 U.S.C. 120, the claims in a U.S. application are entitled to the benefit of the filing date of an earlier filed U.S. application if the subject matter of the claim is disclosed in the manner provided by 35 U.S.C. 112, first paragraph in the earlier filed application. In re Scheiber, 587 F.2d 59, 199 USPQ 782 (CCPA 1978). MPEP § 2163.03.II, page 2100-178, MPEP 8th ed, rev.

2, May, 2004. Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. The subject matter of the claim need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement. MPEP § 2163.02, page 2100-178, MPEP 8th ed, rev. 2, May, 2004.

Thus, it is not necessary for a priority document to provide "specific support in the parent application" to satisfy the requirements of section 112, first paragraph, such that the pending claims can claim priority to the earlier filed specification. The claimed subject matter need not be described in haec verba (literally) in the parent specification to satisfy the description requirement. It is not necessary that the priority document describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that applicants invented the claimed subject matter. In re Herschler, 591 F.2d 693, 700, 200 USPQ 711,717 (CCPA 1979). See also Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed subject matter at issue.").

The Patent Office alleged, inter alia, that claims 93, 101, 103, 117 to 119 and 128 to 130, which recite specific sized nucleic acid fragments and varying percent sequence identities do not find specific support in the parent application (see paragraph 5, page 4, lines 1 to 6 of the OA). However, Applicants respectfully submit that support for claims directed to methods using a nucleic acid having at least about 99%, 98%, 97%, 96%, 95%, 90%, 85%, 80%, 75% or 70% sequence identity to an exemplary sequence of the invention can be found not only in the instant specification (inter alia, page 42, line 15, to page 43, line 2, and on page 56, lines 9 to 24), but also in the parent specification, e.g., see column 8, lines 24 to 38, in USPN 5,789,228:

> The present invention further relates to polynucleotides which hybridize to the hereinabove-described sequences if there is at least 70%, preferably at least 90%, and more preferably at least 95% identity between the sequences. The present invention particularly relates to polynucleotides which hybridize under stringent conditions to the hereinabove-described polynucleotides. As herein used,

> the term "stringent conditions" means hybridization will occur only if there is at least 95% and preferably at least 97% identity between the sequences.

By describing the invention as encompassing nucleic acids having at least 70% sequence identity to exemplary nucleic acids of the invention, the parent application's specification described the claimed invention sufficiently clearly such that one ordinary skill in the pertinent art would recognize from the disclosure that applicants invented the subject matter of the pending claims. Further support in the parent application can be found, inter alia, in column 8, lines 48 to 54, in USPN 5,789,228:

> Thus, the present invention is directed to polynucleotides having at least a 70% identity, preferably at least 90% identity and more preferably at least a 95% identity to a polynucleotide which encodes the enzyme of SEQ ID NO:2 as well as fragments thereof, which fragments have at least 30 bases and preferably at least 50 bases and to enzymes encoded by such polynucleotides.

This paragraph also supports claims directed to nucleic acids encoding an endoglucanase comprising at least 30 (i.e., 30 or more) consecutive residues of a sequence having at least about 95%, 96%, 97%, 98% or 99% sequence identity to an exemplary sequence of the invention (e.g., SEQ ID NO: 1); as this disclosure clearly indicates to the skilled artisan that Applicants invented the claimed subject matter, including 30, 40, 50, 75 or more consecutive residues of an exemplary sequence of the invention. Further support can be found, inter alia, in column 8, lines 39 to 47, of USPN 5,789,228:

> Alternatively, the polynucleotide may have at least 15 bases, preferably at least 30 bases, and more preferably at least 50 bases which hybridize to a polynucleotide of the present invention and which has an identity thereto, as hereinabove described, and which may or may not retain activity. For example, such polynucleotides may be employed as probes for the polynucleotide of SEQ ID NO:1, for example, for recovery of the polynucleotide or as a PCR primer.

Thus, the claimed various sized nucleic acid fragments and nucleic acids of varying percent sequence identities to exemplary sequence of the invention do find sufficient support in the parent application to satisfy the requirements of section 112, first paragraph, and claims 93, 101, 103, 117 to 119 and 128 to 130, reciting specific sized nucleic acid fragments and varying percent sequence identities can claim priority to the parent specification (USPN 5,789,228).

It is also alleged that the parent specification does not provide support for methods of modifying any small molecule because, inter alia, the recitation of small molecule is not specifically defined in the instant specification to be limited to cellulose or carboxymethylcellulose (CMC), and therefore encompasses any carbohydrate, lipid, peptide, nucleic acid or organic or inorganic molecule, while the parent specification only provides support for using the exemplary enzyme of the invention with two small molecule - cellulose and CMC.

The claimed subject matter need not be described in haec verba (literally) in the parent specification to satisfy the description requirement. It is not necessary that the priority document describe the claim limitations exactly, but only so clearly that one having ordinary skill in the pertinent art would recognize from the disclosure that applicants invented the claimed subject matter. As noted by the Office, the parent application provides support for using the enzyme encoded by the exemplary SEQ ID NO:1 with two molecules - cellulose and CMC. Applicants respectfully submit that these two exemplary species were sufficient to support the instantly claimed methods directed to modifying small molecules.

Accordingly, because pending claims 43 to 55, 88 to 93, 95, 96, 101, 103, 106, 107, 110, 112, 115 to 119 and 124 to 133 encompass inventions that were sufficiently clearly conveyed to those skilled in the art at the time the application was filed to satisfy section 112, first paragraph, they were sufficiently described in and can properly claim benefit of priority to the parent application.

Specification

The disclosure is objected to for containing embedded hyperlinks. The instant amendment addresses this issue.

Issues under 35 U.S.C. §112, first paragraph, enablement

Claims 42 to 55, 88 to 96, 101, 103, 106 to 107, 110 to 112 and 115 to 133, are rejected under 35 U.S.C. §112, as allegedly failing to comply with the enablement requirement. It is alleged that the claims contain subject matter which was not described in the specification in such a way as

to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Patent Office is concerned that because the specification does not define endoglucanase activity, the term broadly encompasses any other activity of the polypeptide encoded by SEQ ID NO:1, including antigenic activity (see, e.g., the sentence spanning page 5 to 6, of the OA). The instant amendment addresses this issue. The instant amendment clarifies that the claimed invention encompasses nucleic acids that encode polypeptides having endoglucanase enzymatic activity.

The Patent Office alleges, inter alia, that because the specification provides inadequate guidance to determine which variations of the exemplary SEQ ID NO:1 would be likely to retain biological activity, it would have taken undue experimentation to practice the invention. Applicants respectfully aver that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of polypeptides having endoglucanase or cellulase activity, and the nucleic acids that encode them, to practice the claimed invention – and will provide evidence and expert declaration to support this argument.

However, Applicants respectfully submit that the Patent Office has not met its initial burden to establish a reasonable basis to question the enablement provided for the claimed invention, and as specifically addressed, below, how the art used to support the Office's enablement rejection is not sufficient to rebut the presumptively enabled specification.

In order to make a rejection, the Examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (Examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the

statements contained therein which must be relied on for enabling support. As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). See also MPEP §2164.04, rev. 2, May 2004, pg 2100-189.

The Patent Office cited art to support its *prima facie* case of lack of enablement. Pons, et al. (1997) J. of Biol. Chem. 20:13006-13012 ("Pons"), and Zhang, et al. (1997) J. of Biotechnology 57:101-113 ("Zhang"), were cited to allegedly teach the unpredictability of modifying endoglucanases by site-directed mutagenesis to attain a molecule with any specific activity or ability to modify any cellulose substrate (see, e.g., the paragraph spanning pages 7 and 8, of the OA). Fetrow, et al. (1998) J. Mol. Biol. 282:703-711 ("Fetrow"); and Skolnick (2000) TIBTECH, Jan. 2000, 18:34-39 ("Skolnick"), were cited to allegedly teach the unpredictability of using structural homologies between proteins to predict function (see, e.g., the paragraph spanning pages 8 and 9, of the OA). However, none of these references, individually or in their totality, are sufficient to rebut the presumption of enablement.

Pons and Zhang were cited for allegedly teaching the unpredictability of modifying endoglucanases by site-directed mutagenesis to attain a molecule with any specific activity or ability to modify any cellulose substrate. The Office noted that Pons teaches making mutants of a glucanhydrolase and that some of the mutants had surprising effects that were unpredictable from a simple structural analysis. It was also noted that Pons made a thermostable mutant with properties that would have been unpredictable from current (1997) structure/function relationships. However, while Pons may support the idea that in 1997, one could not predict the exact change in enzymatic activity or stability of a variant resulting from a structural or sequence change, Pons actually supports the idea that it was routine and predictable to use mutagenesis techniques to make and identify active variant enzymes.

Pons used alanine scanning mutagenesis on a beta-glucanase to study the importance of a surface loop structure on the enzyme's activity and stability. Pons demonstrated that both alanine scanning mutagenesis and enzyme activity and stability assays on the resultant enzyme variants were routine procedures – which Applicants note were adaptable to high throughput screening. For example, on page 13009, first column, Pons notes that by using an artificial substrate that produced a chromophore reaction product activity could be continuous monitored. Enzyme stability could also be monitored by fluorescence (see, e.g., page 13007, last paragraph). Not only did Pons predictably and routinely generate active enzyme variants, but several mutants were more thermostable and had higher catalytic activity. It was because this higher activity and increased stability in the variants was not predicted by the specific sequence change that the Office cited Pons to support its allegation of unpredictability – i.e., the alleged unpredictability of modifying endoglucanases by site-directed mutagenesis to attain a molecule with any specific activity or ability to modify any cellulose substrate. However, while the exact nature of the modified activity could not be predicted, Pons did demonstrate that variants could be predictably generated and routinely tested/screened for activity and stability without undue experimentation. In fact, Pons ends its discussion noting "... scanning and random mutagenesis strategies are useful approaches to obtain proteins with improved properties for biotechnological applications" (see page 13011, last sentence).

The Office noted that Zhang teaches that surface residue changes of an endoglucanase had significant changes on the enzyme's substrate specificity. However, as noted by the Office, Zhang in fact teaches that most of the mutants did not show major changes in activity, and those that did show major changes in activity were (predictably) active site mutations. Mutations were made by the routine PCR overlap extension protocol (see, e.g., page 103, section 2.2). Enzyme variants were identified by routine screening protocols (see, e.g., page 106, section 2.4). Structural (secondary structures) changes were monitored by routine circular dichroism studies (see, e.g., page 109, section 3.5). Binding assays were carried out by routine direct fluorescence titration assays (see, e.g., page 106, section 2.7). Applicants note that all of these procedures were adaptable to high throughput analysis. Thus, while Zhang, like Pons, may teach that predictive analysis is not exactly accurate, it did demonstrate that most non-active site mutations did not show major changes

in enzyme activity and site-directed mutagenesis could predictably generate enzyme variants active on multiple substrates that were identifiable by routine screening protocols.

Fetrow and Skolnick were cited to allegedly teach the unpredictability of using structural homologies between proteins to predict function. The Office alleges that Fetrow teaches that "threading" (their software structure prediction program) can identify protein families with similar structures but dissimilar functions, and knowledge of enzyme structure is not equivalent to identification of protein function. In fact, Fetrow demonstrates that by subjecting an entire bacterial genome to their software sequence analyses – a combination of their "threading" and active site residue identification ("FFF") programs – for glutaredoxin/ thioredoxin oxidoreductase sequences, "the combination of [these two programs] can successfully identify the active-site residues ... [and provide] a powerful, new automated method for rapidly screening complete genome sequence databases for specific protein active sites and for identification of the residues of those active sites" (see page 709, first column). Fetrow concludes that their system was "a promising new approach to the prediction of protein activity from sequence ... (see penultimate sentence at end of conclusion, page 709)." Thus, Fetrow teaches an approach to determine active site sequences by software analysis of sequences. Additionally, it appears Fetrow considered the actual "wet lab" screening for enzyme activity routine and predictable.

The Office alleges that Skolnick teaches that because sequence identity between subfamilies is so high, standard sequence similarity methods could easily misclassify new sequences as members of the wrong subfamily if functional sites are not carefully considered. In fact, Skolnick is a Jan., 2000, review article accessing the accuracy of software programs in predicting function from sequences. It concludes that understanding an enzyme's structure allows use of the more accurate "structure to function" paradigm predictor of function. Thus, Skolnick teaches that using paradigms that only consider sequence homologies between proteins may be unpredictable in determining enzyme function(s) – and suggests that additional consideration of structure may result in more successful predictions. Thus, Applicants submit that Fetrow and Skolnick actually support the idea that, while sequence homologies between proteins cannot exactly predict what change in enzyme function may be caused by a structural modification, sequence homology analysis does

provide "powerful" guidance in identifying residues of active sites and other structural elements which may effect enzyme activity.

Applicants respectfully aver that none of these references, individually or in their totality, are sufficient to rebut the instant application's presumption of enablement. None of these references rebut the presumption that one skilled in the art at the time of the invention could have routinely and predictably made and identified endoglucanase-encoding nucleic acid variants, i.e., made the nucleic acids and enzymes of the invention without undue experimentation. In fact, the cited art, particularly Zhang and Pons, actually taught that site-directed mutagenesis could predictably generate enzyme variants active on multiple substrates that were identifiable by routine screening protocols. Fetrow and Skolnick taught that sequence homology analysis provides "powerful" guidance in identifying residues of active sites and other structural elements which may effect enzyme activity.

The Patent Office also alleged that the specification provided insufficient guidance to allow the skilled artisan to determine which of a broad range of possible variations encoded a polypeptide retaining biological activity. In particular, it was alleged that it would have required some knowledge or guidance as to which are the specific structural elements (e.g., domain structures, location active sites, interaction with co-factors or regulatory molecules, secondary and tertiary structure) that correlate with enzyme activity to create variants and test them for activity to enable the skilled artisan to make and use the invention (see, e.g., the section of the OA spanning pages 6 and 7).

However, Applicants respectfully note that the specification does provide guidance as to what amino acid substitutions can be made to make the genus of claimed enzymes. For example, in the paragraph from line 31, page 10 to line 16, page 11, describes

> Additionally a "substantially identical" amino acid sequence is a sequence that differs from a reference sequence by one or more conservative or non-conservative amino acid substitutions, deletions, or insertions, particularly when such a substitution occurs at a site that is not the active site of the molecule, and provided that the polypeptide essentially retains its functional properties. A conservative amino acid substitution, for example,

> substitutes one amino acid for another of the same class (*e.g.*, substitution of one hydrophobic amino acid, such as isoleucine, valine, leucine, or methionine, for another, or substitution of one polar amino acid for another, such as substitution of arginine for lysine, glutamic acid for aspartic acid or glutamine for asparagine). One or more amino acids can be deleted, for example, from an endoglucanase polypeptide, resulting in modification of the structure of the polypeptide, without significantly altering its biological activity. For example, amino- or carboxyl-terminal amino acids that are not required for endoglucanase biological activity can be removed. Modified polypeptide sequences of the invention can be assayed for endoglucanase biological activity by any number of methods, including contacting the modified polypeptide sequence with an endoglucanase substrate and determining whether the modified polypeptide decreases the amount of specific substrate in the assay or increases the bioproducts of the enzymatic reaction of a functional endoglucanase polypeptide with the substrate.

See also page 51, lines 16 to 24, of the specification for further direction in making conservative substitutions. Accordingly, the specification did provide guidance as to what base and residue changes could be made to make the genus of endoglucanase-encoding nucleic acids of the invention. Furthermore, as noted by Dr. Short in the enclosed Rule 132 expert declaration, if the artisan at the time of the invention elected to use elements of enzyme structure for guidance in designing and making variants (e.g., as to which amino acid residues can be substituted, deleted or inserted into a nucleic acid to obtain structural, and functional homologues of an enzyme), the skilled artisan could find such direction in the art at the time of the invention. For example, Dominguez (1996) "The crystal structure of a family 5 endoglucanase mutant in complexed and uncomplexed forms reveals an induced fit activation mechanism," J. Mol. Biol. 257(5):1042-1051, describes the crystal structure of an endoglucanase; Ducros (1995) "Crystal structure of the catalytic domain of a bacterial cellulase belonging to family 5", Structure 3(9):939-49, describes the crystal structure of the catalytic domain of an endoglucanase; Davies (1995) "Structures of oligosaccharide-bound forms of the endoglucanase V from *Humicola insolens* at 1.9 A resolution," Biochemistry 34(49):16210-20, describes the crystal structures of an endoglucanase in various forms. Accordingly, one skilled in the art at the time of the invention using the teaching of the specification had many sources of direction to understand the structure of endoglucanases and have direction and guidance in determining which amino acid residues could be substituted, deleted or

inserted into a nucleic acid to obtain structural and functional variants of the exemplary endoglucanase of the invention.

However, Applicants respectfully aver that it would not have been necessary for one skilled in the art to understand which specific regions of endoglucanase structure could be modified to generate the genus of nucleic acids or polypeptides of the invention. As noted by Dr. Short in the enclosed Rule 132 expert declaration, it would not have required any prior knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with endoglucanase activity to create variants of the exemplary nucleic acid and test them for the expression of polypeptides or peptides having endoglucanase activity.

Dr. Short declares that it would not have been necessary for the skilled artisan to understand which specific regions or structural elements (including, e.g., domain structures, location active sites or sites of interaction with co-factors or regulatory molecules, secondary and tertiary structure) of an endoglucanase were necessary for function or activity to routinely generate the genus of endoglucanase-encoding nucleic acids of the invention. Dr. Short declares that methods for making and screening endoglucanases were sufficiently comprehensive and routine at the time of the invention to predictably generate a genus of endoglucanase-encoding sequences without need of knowing or predicting beforehand which specific regions or structural elements of a sequence or structure affected function or activity. Dr. Short declares that methods known at the time of the invention for modifying nucleic acid and polypeptide sequences in combination with high through-put enzyme (endoglucanase) screening assays made methods that required previous knowledge of structural elements necessary for enzymatic activity obsolete and unnecessary. Dr. Short declares that high through-put enzyme screening methodologies known at the time of the invention (including *in vivo* and *in vitro* nucleic acid expression and enzyme (endoglucanase) screening protocols) made methods that require previous knowledge of protein structure, including secondary or tertiary structure, active site sequences, and the like obsolete and unnecessary. Dr. Short declares that by using methods known in the art at the time of the invention it would not have been necessary to understand which specific regions of enzyme structure (e.g., domain structures, active sites, secondary and tertiary structure) could, or could not, be modified to generate the genus of nucleic

acids of the invention without undue experimentation. Dr. Short declares that the specification provided sufficient guidance to one of ordinary skill in the art to make and use the genus of endoglucanase-encoding nucleic acids to practice the invention.

The Patent Office also alleges that a large quantity of research would be required to make and use the invention (see, e.g., the paragraph spanning pages 10 and 11, of the OA). Applicants respectfully submit that the specification contained sufficient information – a reasonable amount of guidance - regarding making and identifying the claimed genus of polypeptides as to enable one skilled in this art to make and use the claimed invention without undue experimentation.

Enablement is a legal determination of whether a patent enables one skilled in the art to make and use the claimed invention. Raytheon Co. v. Roper Corp., 724 F.2d 951, 960, 220 USPQ 592, 599 (Fed. Cir. 1983). Enablement is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive. Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984); W.L. Gore and Associates v. Garlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315 (Fed. Cir. 1983). Whether large numbers of compositions (e.g., enzymes, antibodies, nucleic acids, and the like) must be screened to determine if one is within the scope of the claimed invention is irrelevant to an enablement inquiry. Experimentation is not considered undue, even if extensive, if it is routine or if the specification provides reasonable guidance regarding the direction of experimentation -- time and difficulty are not determinative of undue experimentation if the experimentation is routine. See PPG Indus., Inc. v. Guardian Indus. Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996); In re Wands, 858 F.2d at 736-40, 8 USPQ2d at 1403-7; Hybritech, Inc. v. Monoclonal Antibodies, Inc.,802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987) (acknowledging that, because practitioners in that art are prepared to screen large numbers of negatives in order to find a sample that has the desired properties, the screening that would be necessary to make additional antibody species was not "undue experimentation."). Thus, enablement is not precluded by the necessity to screen large numbers of compositions, as long as that screening is "routine," i.e., not "undue," to use the words of the Federal Circuit.

Analogously, practitioners of the biological sciences for the instant invention also recognized the need to screen numbers of negatives to find a sample that had the desired properties, e.g., a desired endoglucanase or cellulase activity. As declared by Dr. Short, the screening procedures used to make and identify nucleic acids and polypeptides of the invention, including high throughput screening assays, were all well known in the art at the time the application was filed. These procedures provided routine protocols for the skilled artisan that yielded predictably positive results – making and identifying endoglucanase enzymes having a desired activity. Furthermore, as noted above, the specification contained sufficient information – a reasonable amount of guidance - regarding making and identifying the claimed genus of polypeptides as to enable one skilled in this art to make and use the claimed invention. Thus, the skilled artisan using Applicants' written disclosure could make the claimed genus of nucleic acids and polypeptides without undue experimentation.

Accordingly, Applicants respectfully submit that the pending claims meet the enablement requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Issues under 35 U.S.C. §112 second paragraph

Claims 90 to 92 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The instant amendment addresses this issue.

Issues under 35 U.S.C. §102

Claims 88, 89, 93, 95, 96, 101, 103, 106, 107, 110, 112, 115, 117 to 119 and 124 to 133 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Lam, et al., U.S. Patent No. 6,074,867, issued June 13, 2000, and filed October 15, 1997 ("the '867 patent").

As discussed above, Applicants respectfully submit that claims 88, 89, 93, 95, 96, 101, 103, 106, 107, 110, 112, 115, 117 to 119 and 124 to 133, can properly claim benefit of priority to the parent application, U.S. patent application serial no. (USSN) 08/651,572, filed May 22, 1996,

now U.S. Patent No. (USPN) 5,789,228. Because the '867 patent is not prior art to pending claims 88, 89, 93, 95, 96, 101, 103, 106, 107, 110, 112, 115, 117 to 119 and 124 to 133, the rejection of these claims under 35 U.S.C. §102(b) can be properly withdrawn.

Applicants also note that the cited '867 patent is a divisional application of the instant (CIP) application's priority document, i.e., the cited '867 patent is a divisional of (having the same specification as) the parent application USSN 08/651,572.

The Office has alleged that claims 43 to 55, 88 to 93, 95, 96, 101, 103, 106, 107, 110, 112, 115 to 119 and 124 to 133, cannot claim priority to the parent application USSN 08/651,572, which has the same disclosure as the cited '867 patent. However, the Office has also alleged that claims 43 to 55, 88 to 93, 95, 96, 101, 103, 106, 107, 110, 112, 115 to 119 and 124 to 133, are anticipated by the cited '867 patent, which has the same disclosure as the parent application USSN 08/651,572. In other words, the Office is alleging that a disclosure which does not provide sufficient support under section 112, first paragraph, to be a priority document can at the same time be a disclosure that anticipates the same claims.

While Applicants maintain that the disclosure of the parent application USSN 08/651,572 (the same disclosure as the cited '867 patent) does provide sufficient support under section 112, first paragraph, to be a priority document for claims 43 to 55, 88 to 93, 95, 96, 101, 103, 106, 107, 110, 112, 115 to 119 and 124 to 133, if *arguendo* the Office's allegation the USSN 08/651,572 (and the '867 patent) disclosure did not provide sufficient support under section 112, first paragraph, were true – then this same disclosure cannot be also be an anticipatory reference, and the rejection of the claims under 35 U.S.C. §102(b) should be withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs, and 35 U.S.C. §102. Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952 referencing attorney docket no. 564462000520. Please credit any overpayment to this account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at (858) 720-5133.

Dated: February 3, 2005

Respectfully submitted,

By _____

Gregory P. Einhorn
Registration No.: 38,440
MORRISON & FOERSTER LLP
3811 Valley Centre Drive, Suite 500
San Diego, California 92130
(858) 720-5133